Pharmahuasca: Human Pharmacology of Oral DMT Plus Harmine†

Jonathan Ott*

Abstract—A summary is presented of human self-experiments or *psychonautic bioassays* of *pharmahuasca*—capsules containing crystalline N,N-dimethyltryptamine (DMT) plus harmine, as well as combinations of other psychoactive tryptamines with other β-carbolines. The 1967 Holmstedt–Lindgren hypothesis of the *ayahuasca effect*—oral psychoactivity of DMT consequent to monoamine-oxidase (MAO) inhibition from simultaneous ingestion of β-carbolines—has been confirmed by eight self-experimenters. Results of a total of some 70 bioassays are summarized and the literature on this subject is reviewed (with 66 references and one table).

Keywords—*ayahuasca*; β-carbolines; N,N-dimethyltryptamine; harmine; 5-methoxy-N,N-dimethyltryptamine; monoamine-oxidase-inhibitors (MAOI)

A 1967 analysis of a half-dozen South American snuffs used in shamanic healing by the Tucano, Waiká, Araraibo, Piaroa and Surára Indians, showed all but one of the powders to contain tryptamines, mainly 5-methoxy-N,N-dimethyltryptamine (5-MeO-DMT) and secondarily N,N-dimethyltryptamine (DMT) (Holmstedt & Lindgren 1967). However, a *paricá* snuff of the Piaroa Indians of the Venezuelan Orinoco region contained tryptamines—5-OH-DMT (bufotenine), DMT and 5-MeO-DMT—together with the β-carboline alkaloid harmine. An *epéna* snuff of the Surára Indians contained only β-carbolines; this had previously been reported in the same Surára *epéna* (Bernauer 1964) and in a Tucano Indian sample of *paricá* snuff (Biocca et al. 1964). Since bufotenine and DMT appeared to be nonpsychoactive intranasally (Turner & Merlis 1959), Holmstedt and Lindgren (1967: 365) commented:

> The occurrence of both tryptamines and β-carbolines in the South American snuffs is pharmacologically interesting. The β-carbolines are monoamine-oxidase inhibitors, and could potentiate the action of the simple indoles. The combination of β-carbolines and tryptamines would thus be advantageous.

The following year, Holmstedt and Lindgren, in collaboration with Agurell, found DMT in leaves of *Diplopterys cabrerana* (Cuatrecasas) Gates (Malpighiaceæ) used as an admixture to *ayahuasca* or *yajé* by Ecuadorian Kofán Indians (Agurell, Holmstedt & Lindgren 1968), a finding replicated by Der Marderosian, Pinkley and Dobbins IV (1968). *Ayahuasca* is a pan-Amazonian complex of shamanic potions based on aqueous infusions of the stem

†The author is beholden to Drs. James C. Callaway, Mark S. Donnell, Jochen Gartz, Robert Montgomery and Alexander T. Shulgin for discussions and advice. This paper is dedicated to Professor Richard Evans Schultes of Harvard University, in grateful recognition of his pioneering role in elucidating the botany and ethnopharmacognosy of *ayahuasca* potions.

*President, Natural Products Company, Xalapa, Veracruz, México.

Please address correspondence and reprint requests to Jonathan Ott, President, Natural Products Company, Apartado Postal 532, Xalapa, Veracruz, México. Telefacsimile: [011] 522—814–4085.

of the *ayahuasca* liana *Banisteriopsis caapi* (Spruce ex Griseb.) Morton (Malpighiaceæ), to which may be added visionary, stimulant or curative admixture plants, some 100 of which have been identified (Ott 1995c; 1994; 1993). Three years earlier, Jacques Poisson had isolated DMT from dried leaves of *D. cabrerana* (in all three of these reports the synonym *Banisteriopsis rusbyana* [Niedenzu] Morton was used) added to *natem[a]* or *ayahuasca* by Ecuadorian Shuar Indians (Poisson 1965). Later research documented widespread use of DMT-rich leaves of *Psychotria viridis* Ruiz et Pavón (Rubiaceæ) in *ayahuasca* potions (Ott 1994). Agurell, Holmstedt, and Lindgren (1968: 148) extended the earlier observation regarding the snuffs to *ayahuasca*, noting: "The combination in yajé of monoamine oxidase inhibiting harman alkaloids with N,N-dimethyltryptamine might result in specific pharmacological effects," an observation echoed by Der Marderosian, Pinkley and Dobbins IV (1968: 146).

This hypothesis of DMT/β-carboline synergy was proposed to account for presumed oral activity of DMT in *ayahuasca* potions. Although this idea was first suggested in relation to the snuffs, this has been all but forgotten; there have been only rudimentary attempts to model the psychoactivity of the snuffs with pure compounds, although such studies are underway and will be reported in due course. DMT, first synthesized in 1931 (Manske 1931) and first isolated from *Anadenanthera peregrina* (L.) Speg. (Leguminosæ) seeds used to prepare *cohoba* snuff 24 years later (Fish, Johnson & Horning 1955), was found to be inactive orally in doses as high as 1.0 gram (*ca.* 13.0 mg/kg; Shulgin 1976), although it was dramatically psychoactive via intramuscular (IM) injection in doses of 30 to 150 mg (0.4–2.0 mg/kg; Szára 1957), seems to be quite as active when inhaled as vaporized free-base (0.4–0.5 mg/kg highly active; Ott 1993), and more active still when injected intravenously (0.2–0.4 mg/kg IV was said to be "hallucinogenic"; Strassman & Qualls 1994; Strassman et al. 1994). According to the ingenious Holmstedt–Lindgren hypothesis, the β-carbolines present in *ayahuasca* potions were serving to inhibit the catabolic enzyme monoamine-oxidase (MAO)—which would normally metabolize oral DMT before it could get from the digestive system to the brain—so allowing the DMT also present in the *ayahuasca* potions to be absorbed and transported in the circulation to the brain, there evoking visionary, psychotropic effects. It is a matter of conjecture how the Amazonian Indians might have learned that the orally-inactive leaves of *Diplopterys* and *Psychotria* could be transformed into visionary agents by combination with stems of *Banisteriopsis caapi.*

The Holmstedt–Lindgren theory—what we might call the *ayahuasca effect*—won wide acceptance in the literature, for it neatly explained the visionary effects of *ayahuasca*. These effects could hardly have been due to the β-carbolines alone, which elicit rather a sedative, Valium-like psychoactivity, and have a high threshold for oral activity—8.0 mg/kg in the case of harmine, the main alkaloid of *ayahuasca* plants and potions (Naranjo 1967). Plants rich in β-carbolines have found world-wide use as sedatives, a property experimentally verified (Monardes 1990; Moore 1989; Speroni & Minghetti 1988; Oga et al. 1984). On the other hand, four reported analyses of 16 *ayahuasca* potions showed an average of 158 mg β-carbolines per dose (range: 20–401 mg/dose); there were generally three parts harmine to one part *d*-leptaflorine (*R*-1,2,3,4-tetrahydroharmine), with traces of harmaline (3,4-dihydroharmine). This would amount to just over two mg/kg (racemic leptaflorine was found to be even less active than harmine, with an oral threshold of 12 mg/kg) (Liwszyc et al. 1992; McKenna, Towers & Abbott 1984; Rivier & Lindgren 1972; Der Marderosian et al. 1970; Naranjo 1967). Since the β-carbolines *per se* could not explain the legendary psychoptic (visionary) activity of the jungle ambrosia, this had to be due to its DMT content, which amounted to an average of 29 mg/dose in the 16 potions analyzed (range: 25–36 mg/dose). Accordingly, the Holmstedt–Lindgren theory won the day (see Ott 1994, for details and analysis of the phytochemistry of *ayahuasca* plants and potions, summarized in Tables II-A, II-B and II-C).

Nevertheless, this well-accepted theory had not been tested, either *in vitro* or *in vivo*, and remained nothing but a logical explanation of quite scanty phytochemical and pharmacological data. Sixteen years passed before McKenna, Towers & Abbott (1984) showed that two Peruvian *ayahuasca* samples were "extremely effective" MAO-inhibitors *in vitro* (in a rat-liver cytosol fraction) as was an *ayahuasca* analogue—a solution of a mixture of 69% harmine, 26% leptaflorine (probably racemic) and 4.6% harmaline, that mimicked proportions that had been found in *ayahuasca* potions. So *ayahuasca* was decidedly an MAO-inhibitor, but it remained to be seen whether the sum total of all β-carbolines present in a typical dose of the potion (158 mg) could render psychoactive in a human subject the 25 to 36 mg (average: 29 mg) of DMT also present. Only human self-experiments (psychonautic bioassays), known as the "Heffter Technique" (Ott 1995d) could establish this with certainty, in the alembic of the human brain (McKenna, Towers & Abbott 1984).

When I began to investigate this question in 1990, I was able to build on the rudimentary experiments of Bigwood and Gracie and Zarkov. Bigwood made a single bioassay of *pharmahuasca*—a capsule containing 100 mg each of DMT free-base (1.16 mg/kg) and harmaline hydrochloride (=86 mg freebase; 1.0 mg/kg), noting: "DMT-like hallucinations . . . very similar to . . . a DMT- and harmaline-containing *ayahuasca* brew that I had previously experimented with" (Bigwood 1978). While this single experiment seemingly confirmed the Holmstedt–Lindgren theory, nonetheless it was conducted with some three to four times the amount of DMT found in typical

doses of *ayahuasca*, and the β-carboline chosen (harmaline) "does not contribute significantly" to the pharmacology of the potions (McKenna, Towers & Abbott 1984: 221). Subsequent "underground" experiments by Gracie and Zarkov (1986) found DMT to be active orally in combination with aqueous infusions of β-carboline-rich seeds of *Peganum harmala* L. (Zygophyllaceæ, traditionally used as hypnotics; Kirtikar et al. 1935). The threshold level was 20 mg DMT, with 30 or 40 mg being a preferred dose (Gracie & Zarkov 1986). Taken together, these pioneering experiments provided tentative, albeit fragmentary, confirmation of the hypothesized *ayahuasca effect*, but it seemed to me desirable to conduct more systematic psychonautic bioassays of *pharmahuasca* using measured amounts of both pure DMT and β-carbolines. Accordingly, for such psychonautic bioassays, I isolated and purified DMT (as freebase, mp 45,° characterized by thin-layer chromatographic comparison with reference sample) from roots of *Desmanthus illinoensis* (Michaux) MacM. (Leguminosæ), and harmine (as the hydrochloride salt, mp 262,° characterized by TLC comparison with authentic reference) from seeds of *Peganum harmala*, using standard alkaloid-purification techniques as outlined in the literature (McKenna, Towers & Abbott 1984; Manske 1952). Both plants were obtained commercially on the U.S. herb market. All bioassays were conducted outside of the United States, with standard "double-conscious" procedure, as described by Shulgin and Shulgin (1991: XXVII). Double-conscious, a term introduced by Gordon Alles, means simply that the human-bioassay subject be informed both regarding the identity (as well as the dosage) of the drug being tested, and also as to the nature of the effects which might be anticipated.

In a total of some three dozen experiments (most of which are detailed in Ott 1994), I was able to confirm *in vivo* the Holmstedt–Lindgren *ayahuasca effect*, in my own body. I found that DMT was indeed rendered psychoactive orally in combination with harmine hydrochloride taken simultaneously in a single gelatin capsule. Starting with quantities near the lowest levels found in *ayahuasca* potions (20 mg DMT and 40 mg harmine), I systematically tested increasing doses. I found 120 mg of harmine (expressed as the freebase; 1.5 mg/kg) to be the threshold for the *ayahuasca effect*, whereas in a control experiment with this amount without DMT, barely-perceptible sedative effects resulted—harmine hydrochloride has been characterized as a "stupefying" agent (Font Quer 1993: 424). Although I could feel 20 mg DMT (0.25 mg/kg) combined with 120 mg harmine, for me the visionary or psychoptic threshold level was 30 mg DMT (0.38 mg/kg). I have tested doses as high as 160 mg DMT (2.0 mg/kg), experiencing progressively more intense psychotropic effects, but always with the same approximate pharmacodynamics. The effects were quite similar to what I have enjoyed with genuine Amazonian *ayahuasca* potions in Brasil, Ecuador and Perú—45 minutes to an hour incubation period, with effects quickly building to a peak within the next 30 minutes and maintaining a plateau for 45 minutes to an hour, followed by about an hour of diminishing effects; the experience was usually completely over within three hours. In no case have I ever experienced nausea in *pharmahuasca* experiments, although I have weathered nausea and episodes of vomiting provoked by genuine *ayahuasca* in Amazonia. In any case, I generally eat little or nothing on the day of ingestion. During the experimental series, I always allowed roughly a minimum of a week to elapse between the individual experiments.

I have been able to extend these observations, based on the experiences of eight psychonauts in all, involving a total of about 70 self-experiments. As some of the experimenters wished to remain anonymous, I will merely cite the sole published account and one personal communication (Callaway 1992; Markus 1989). In all cases double-conscious self-experiments were involved; in no case were the compounds administered to anybody else; and no nonhuman animal experimentation of any kind was conducted.

It was found that both harmaline and 6-methoxy-harmalan (Markus 1989) could substitute for harmine in *pharmahuasca*, at approximately commensurate doses—Callaway found 70 mg harmaline (as freebase; 1.2 mg/kg) to activate tryptamines in *pharmahuasca*, close to the level Bigwood had found active (1.0 mg/kg) (Callaway 1992; Bigwood 1978). Another psychonaut found 175 mg harmaline hydrochloride (146 mg base; 2.25 mg/kg) alone to be a mild sedative. Chemical analysis showed the aged commercial sample of harmaline used had partially oxidized to harmine, being in reality a mixture of some two-thirds harmaline and one-third harmine (Shulgin 1993). Three different dose levels of this "harmaline'" were then tested in combinations with relatively high doses of tryptamines. Whereas a 50 mg dose (43 mg base; 0.66 mg/kg) was not effective as tryptamine activator, doses of 100 mg (86 mg base; 1.32 mg/kg) and 150 mg (130 mg base; 2.0 mg/kg) definitely were. Thus it would appear that for harmaline, too, there is a threshold for activity in *pharmahuasca*, somewhere around 1.0 mg/kg. The doses of 6-methoxy-harmalan found to be effective were not divulged to us in the sketchy second-hand report (Markus 1989).

Callaway (1992) found 10 mg of 5-methoxy-N,N-dimethyltryptamine (5-MeO-DMT) to be psychoactive in *pharmahuasca* (expressed as freebase; 0.17 mg/kg); Markus (1989) also found this compound psychoactive but we do not know the dose. Thus it would appear that 5-MeO-DMT is several times as active as DMT in *pharmahuasca*; mirroring the higher activity of this compound by other routes. Shulgin (1983; 1970) found 5 to 10 mg doses psychoactive by inhaling the vapor of the freebase (0.07–0.13 mg/kg). The artificial compound N,N-diethyltryptamine (DET or

T-9) was likewise found to be psychoactive orally in *pharmahuasca* capsules by two psychonauts, who employed doses of 60 mg freebase (0.7 mg/kg) and 150 mg freebase (2.3 mg/kg) respectively. The latter quantity was characterized as "definitely an overdosage." We lack enough data to speculate on oral threshold levels of DET—it is likely this compound is roughly equipotent with DMT in *pharmahuasca*, much as it is via intramuscular injection. Szára (1957) found 60 mg DET (0.8 mg/kg) psychoactive taken IM; Böszörményi, Dér and Nagy (1959) found it active in doses of from 0.65–0.85 mg/kg IM. A recent book (Shulgin & Shulgin 1997) gives full details of the chemistry and human pharmacology of the β-carbolines and tryptamines discussed here, along with some further *pharmahuasca* data. Whereas 20 and 50 mg of harmaline were insufficient orally to activate 55 and 60 mg of DMT respectively, 80, 100, 150 and 150 mg of harmaline did activate 40, 120, 35 and 80 mg of DMT respectively. Moreover, 70, 80 and 150 mg of harmaline sufficed orally to activate 10, 10 and 25 mg of 5-MeO-DMT respectively. On the other hand, it was noted that harmine (as HCl? 141 mg=120 mg base) could activate 35 to 40 mg of DMT taken orally, in doses in the 140 to 190 mg range; whereas doses of 120 to 140 mg harmine were ineffective when taken with 30 mg of DMT.

These results with *pharmahuasca* have also been extended to so-called "*ayahuasca* analogues" or *anahuasca*—the use of nontraditional source plants for either or both tryptamines and b-carbolines. Since well over 100 plant species in 27 families are known to contain simple β-carbolines (Allen & Holmstedt 1980), some 70 of which contain known MAO-inhibitors (Ott 1994), and some 74 species in 14 families are reported to contain DMT and/or 5-MeO-DMT (Ott 1994; Smith 1977), there are theoretically several thousand combinations of two plants which could provoke the *ayahuasca* effect. Indeed, such *ayahuasca* analogues have lately been made from a variety of plants, although apparently only in Amazonia was the *ayahuasca* effect exploited in archaic ethnomedicine. Always used as source of β-carbolines are the seeds of harmel, Syrian rue or *Peganum harmala*, which are sold worldwide for use as dyestuffs and as incense; the plant is naturalized in North America and Europe (Ott 1994; Gracie & Zarkov 1986; Hassan 1967). Since these seeds contain much higher levels of β-carbolines than do stems of *Banisteriopsis caapi* ordinarily used in *ayahuasca* (2–7% alkaloids, as opposed to an average of 0.45%; Ott 1994; McKenna, Towers & Abbott 1984; Shamma and Abdul-Ghany 1977; Rivier & Lindgren 1972; Poisson 1965), as little as two to three grams of harmel seeds will suffice per dose of *anahuasca*. Although this dose level serves to activate pure DMT or tryptamines in plants added to the *ayahuasca* analogue, an aqueous infusion of 15 grams of harmel seeds without additives acted as a sedative, with no visionary effects (Ott 1995c).

Various sources of tryptamines have been used in these analogues, such as roots of *Desmanthus illinoensis*, *Acacia phlebophylla* F. von Muell. leaves (Leguminosæ); and halms (grass "leaves") of various strains of *Phalaris* spp. (Gramineæ) (Ott 1995a; Festi & Samorini 1993[4]). Presently one of the more widely-used sources of *anahuasca* tryptamines is root-bark of *Mimosa tenuiflora* (Willd.) Poir.—previously known as*M. hostilis* (Mart.) Benth. (Leguminosæ)—source of the *ayahuasca*-like Brazilian traditional entheogen *vinho da jurema*, from which DMT may first have been isolated in 1946 under the presumed synonym nigerine (*nigerina*; Gonçalves de Lima 1946). This commercially-available and well-known ethnomedicine is a rich source of DMT, nearly 0.6% having been isolated from roots (Pachter, Zacharias & Ribeiro 1959); which is, again, more concentrated than the leaves of the *Diplopterys* and *Psychotria* species traditionally used as tryptamine sources in Amazonian *ayahuasca* (average DMT content of 11 samples analyzed: 0.20%; see Table II-B in Ott 1994: 40; McKenna, Towers & Abbott 1984; Rivier & Lindgren 1972; Der Marderosian et al. 1970). Although said to be extinct in Brazil (Schultes & Hofmann 1980) *vinho da jurema* use continues among the Kariri-Shoko (Novaes da Mota 1987), and is presently the focus of laboratory investigations and fieldwork in coastal Brazil.

It has lately been alleged that the *ayahuasca* effect constitutes "potentiation" of tryptamines by β-carbolines, as originally suggested with regard to the snuffs (Holmstedt & Lindgren 1967). In a review article, for example, Callaway (1995:25) noted: "It is well known that βCs potentiate the activity of methylated tryptamines." However, the orally-active DMT in *pharmahuasca* seems to be weaker than that taken via other routes of administration. It would appear that the descending order of potency via distinct routes is: IV injection > inhalation of vapor > IM injection > subcutaneous injection > orally in *pharmahuasca*. Intravenous injection as the fumarate salt appears to be the most effective route; 0.2 to 0.4 mg/kg was described as "hallucinogenic," with the higher quantity seemingly representing the maximum effects of the drug (Strassman & Qualls 1994: 86). Inhalation of the vaporized free-base has a threshold of activity in the 0.2 to 0.4 mg/kg range (Bigwood & Ott 1977), and 40 to 50 mg was described as a "large dose" (0.5–0.7 mg/kg; Meyer 1992: 154); whereas Shulgin (1976: 167) noted 30 mg (0.4 mg/kg) evoked a "complete psychedelic experience." While psychoactivity was observed with intramuscular injection of 30 mg or 0.4 mg/kg (as hydrochloride salt; this dose was misstated as 0.2 mg/kg), 0.7 to 1.0 mg/kg was described as the "optimum" IM dose (Szára 1957: 461); and experienced users found 1.0 mg/kg IM (as fumarate salt) "significantly less . . . hallucinogenic than . . . previous experience with the smoked drug" (Strassman & Qualls 1994: 86). Another researcher characterized the IM

TABLE 1
Human Pharmacology of Psychoptic Tryptamines

Compound/route	Doses (mg/kg) Range	Threshold	Maximal	References
1. DMT, IV	0.05–0.40	0.2	0.4	Strassman & Qualls 1994; Strassman et al. 1994
2. DMT, vapor	0.06–1.00	0.2–0.4	1.0	Meyer 1992; Bigwood & Ott 1977
3. DMT, vapor	0.00–0.40	?	0.4	Shulgin 1976
4. DMT, IM	0.00–2.00	0.4	1.5	Szára 1957
5. DMT, IM	0.50–1.00	0.6	1.0+	Sai-Halász et al. 1958; Sai-Halász 1962
6. DMT, IM	?	0.4	0.7–0.9	Shulgin 1976
7. DMT, SC	0.00–1.00	?	1.0	Shulgin 1976
8. DMT, PO	0.00–13.00	—	—	Shulgin 1976
9. DMT, PH	0.25–2.00	0.4	2.0+	Ott 1993 [1996]
10. DMT, IN	0.07–0.28	—	—	Turner & Merlis 1959
11. DMT, IR	1.70–1.70	—	—	de Smet 1983
12. DET, IM	0.00–0.85	0.65–0.85	?	Böszörményi et al. 1959
13. DET, PH	0.70–2.30	0.7	2.3	Ott 1993 [1996]
14. 5-MD, vapor	0.00–0.13	0.07–0.13	?	de Smet 1983
15. 5-MD, PH	0.17–0.17	0.17	?	Ott 1994

IV= intravenous; IM = intramuscular; SC= subcutaneous; PO = peroral; PH = pharmahuasca; IN = intranasal; IR= intrarectal; 5-MD = 5-MEO-DMT

dose range as 0.75 to 1.0 mg/kg, fixing the threshold level at 0.60 mg/kg: "there are no symptoms at all on administering only 0.50–0.55 mg/kg" (Sai-Halász 1962: 137; Sai-Halász, Brunecker & Szára 1958). Shulgin pegged an "abrupt threshold of activity" at 30 mg (0.4 mg/kg) and estimated that 50 to 70 mg IM (0.7–0.9 mg/kg) provoked the "complete psychedelic experience." Shulgin (1976: 167) gave 75 mg (1.0 mg/kg) as the equivalent "complete" dose via subcutaneous injection. We have seen that the oral DMT threshold in *pharmahuasca* is about 0.3–0.4 mg/kg, and I would estimate that maximum effects would require doses in excess of 2.0 mg/kg. Intranasal DMT freebase was inactive in doses of 5 to 20 mg (0.07–0.28 mg/kg; Turner & Merlis 1959); likewise inactive were doses of up to 125 mg DMT rectally (as a solution of 185 mg bioxalate salt; 1.7 mg/kg; de Smet 1983). These psychonautic bioassay data are summarized in Table 1.

While the β-carbolines clearly render DMT active orally, we can hardly characterize this as potentiation. Indeed, it was demonstrated more than 30 years ago that the artificial MAO-inhibitor iproniazid markedly *inhibited* psychoactive effects of DMT. In subjects given 0.35 to 0.83 mg/kg DMT IM, *greatly reduced* psychoactivity was experienced when the injections were repeated two days after having received 100 mg iproniazid daily for four days: "the DMT psychosis . . . was less pronounced: there were illusions and hallucinations, but without colours, or only with a few of them, and only having the eyes closed" (Sai-Halász 1963: 386). The following year, pretreatment with the MAO-inhibitor isocarboxazid "very markedly attenuated" or entirely blocked effects of oral LSD-tartrate (subjects each received LSD in doses of 40 and 75 mcg; then both doses after two weeks of isocarboxazid, 30 mg/day; both again after five weeks of isocaboxazide treatment; Resnick, Krus & Raskin 1964: 1211). The MAOI nialamide also "blocked" effects of LSD (Grof & Dytrych 1965). A survey conducted by researchers at the U.S. National Institute of Mental Health found: "decrease in response to LSD . . . in those people who had been taking an MAO inhibitor" (Bonson, Buckholtz & Murphy 1996; Bonson 1994: 9). It is interesting to note that in a single experiment I found pretreatment with isocarboxazid (Marplan®), in three doses of 10 mg in a single day, to render psychoactive 30 mg DMT freebase ingested an hour after the final dose of this artificial MAO-inhibitor (Ott 1994).

It would thus appear that the locus of the *ayahuasca* effect is peripheral and that the MAO-inhibitors

which catalyze oral activity of DMT may exert a sort of DMT-blocking effect in the brain. While MAOI can render DMT and other tryptamines active when taken orally, they appear to render it far less potent than when administered via other routes, thus serving as *activators*, but not *potentiators*. We have seen that long-term, daily administration of medicinal MAO-inhibitors (which theoretically elevates brain serotonin levels) can partially or completely block the effects of both DMT and LSD. This has been documented experimentally and also in surveys of patients undergoing daily MAOI therapy. Conversely, the potent serotonin-antagonist methysergide or UML-491 (Sansert®) had "a very strong potentiating effect" on IM DMT (Sai-Halász 1962: 138), at oral (1–2 mg) or IM (0.5 mg) doses well below its own threshold for psychoactivity (4.3 mg; Abramson & Rollo 1967).

Possible DMT-attenuating actions of MAOI might have some bearing on the fact that DMT taken orally in *pharmahuasca* appears to be significantly weaker than that taken via other routes of administration. Strangely, and quite at odds with the limited data at our disposal, the *Peganum harmala* seeds used in *anahuasca* have acquired the reputation of all-purpose pan-potentiators of shamanic inebriants, and have been combined by avid "basement shamans" (contemporary, nontraditional aficionados of shamanic inebriants) with psilocine (4-OH-DMT)-containing mushrooms, LSD, and even leaves of *Salvia divinorum* Epling et Játiva (Labiatæ)—the visionary principle of which, the diterpene salvinorin A, is not even an amine (Ott 1996; 1995b; Siebert 1994)! Nevertheless, this ingenious discovery by South American Indians of the *ayahuasca* effect—conceivably the most sophisticated pharmacognostical discovery ever made in the archaic world—bids fair to revolutionize contemporary, nontraditional entheobotany of visionary shamanic inebriants (Ott 1997).

REFERENCES

Abramson, H.A. & Rollo, A. 1967. Comparison of LSD with methysergide and psilocybin on test subjects. In: H.A. Abramson (Ed.) *The Use of LSD in Psychotherapy and Alcoholism*. New York: Bobbs Merrill.

Agurell, S.; Holmstedt, B. & Lindgren, J.E. 1968. Alkaloid content of *Banisteriopsis rusbyana*. *American Journal of Pharmacy* 140 (5): 148–51.

Allen, J.R.F. & Holmstedt, B.R. 1980. The simple β-carboline alkaloids. *Phytochemistry* 19: 1573–82.

Bernauer, K. 1964. Notiz über die Isolierung von Harmin und (+)-1,2,3,4-Tetrahydro-harmin aus einer indianischen Schnupfdroge. *Helvetica Chimica Acta* 47 (4): 1075–77.

Bigwood, J. 1978. Personal communications. Shelton, Washington.

Bigwood, J. & Ott, J. 1977. DMT: The fifteen minute trip. *Head*. November: 56 *et seq*.

Biocca, E.F.; Galeffi, C.; Montalvo, E.G. & Marini-Bettòlo, G.B. 1964. Sulla sostanze allucinogene impiegata in Amazonia. Nota I. Osservazioni sul paricá dei Tukâno e Tariâna del bacino del Río Uaupés. *Annali di Chimica* 54: 1175–78.

Bonson, K.R.; Buckholtz, J.W. & Murphy, D.L. 1996. Chronic administration of serotonergic antidepressants attenuates the subjective effects of LSD in humans. *Neuropsychopharmacology* 14 (6): 425–36.

Bonson, K. 1994. Psychedelics and psychiatric drugs: National Institute of Mental Health update. *MAPS Bulletin* V (1): 9.

Böszörményi, Z.; Dér, P. & Nagy, T. 1959. Observations on the psychotogenic effect of N-N diethyltryptamine, a new tryptamine derivative. *Journal of Mental Science* 105: 171–81.

Callaway, J.C. 1995. Endogenous β-carbolines and other indole alkaloids in mammals. *Integration: Zeitschrift für Geistbewegende Pflanzen und Kultur* 5: 19–33.

Callaway, J.C. 1992. Personal communications. San Luis Potosí, México and letter dated 4 December.

Der Marderosian, A.H.; Kensinger, K.M.; Chao, J.-M. & Goldstein, F.J. 1970. The use and hallucinatory principles of a psychoactive beverage of the Cashinahua tribe (Amazon basin). *Drug Dependence* 5: 7–14.

Der Marderosian, A.H.; Pinkley, H.V. & Dobbins IV, M.F. 1968. Native use and occurence [*sic*] of N,N-dimethyltryptamine in the leaves of *Banisteriopsis rusbyana*. *American Journal of Pharmacy* 140 (5): 137–47.

de Smet, P.A.G.M. 1983. A multidisciplinary overview of intoxicating enema rituals in the western hemisphere. *Journal of Ethnopharmacology* 9 (2,3): 129–66.

Festi, F. & Samorini, G. 1993[4]. Alcaloidi indolici psicoattivi nei generi *Phalaris* e *Arundo* (*Graminaceae*) [*sic*]: Una rassegna. *Annali dei Musei Civici di Rovereto* 9: 239–87.

Fish, M.S.; Johnson, N.M. & Horning, E.C. 1955. Piptadenia alkaloids. Indole bases of *P. peregrina* (L.) Benth. and related species. *Journal of the American Chemical Society* 77: 5892–95.

Font Quer, P. 1993. *Plantas Medicinales: El Dioscórides Renovado*. Barcelona: Editorial Labor.

Gonçalves de Lima, O. 1946. Observações sôbre o "vinho da Jurema" utilizado pelos índios Pancarú de Tacaratú (Pernambuco). *Arquivos do Instituto do Pesquisas Agronómicas* 4: 45–80.

Gracie & Zarkov 1986. An Indo-European plant teacher. *Notes from the Underground* 10: 1–5.

Grof, S. & Dytrych, Z. 1965. Blocking of the LSD reaction by premedication with Niamid. *Activitas Nervosa Superior* [Prague] 7: 306.

Hassan, I. 1967. Some folk uses of *Peganum harmala* in India and Pakistan. *Economic Botany* 21 (4): 384.

Holmstedt, B. & Lindgren, J.-E. 1967. Chemical constituents and pharmacology of South American snuffs. In: D.H. Efron; B. Holmstedt & N.S. Kline (Eds.) *Ethnopharmacologic Search for Psychoactive Drugs*. Washington, DC: U.S. GPO.

Kirtikar, K.R.; Basu, B.D.; An, I.C.S.; Blatter, E.; Caius, J.F. & Mhaskar, K.S. 1935. *Indian Medicinal Plants*. Volume III. Allahabad, India: Lalit Mohan Basu.

Liwszyc, G.E.; Vuori, E.; Rasanen, I. & Issakainen, J. 1992. Daime—A ritual herbal potion. *Journal of Ethnopharmacology* 36 (1): 91–92.

McKenna, D.J.; Towers, G.H.N. & Abbott, F. 1984. Monoamine oxidase inhibitors in South American hallucinogenic plants: Tryptamine and β-carboline constituents of *ayahuasca*. *Journal of Ethnopharmacology* 10 (2): 195–223.

Manske, R.H.F. 1952. *The Alkaloids*. Volume II. New York: Academic Press.

Manske, R.H.F. 1931. A synthesis of the methyl-tryptamines and some derivatives. *Canadian Journal of Research* 5: 592–600.

Markus, M. 1989. Cited in Leuner, H. & Schlichting, M. A report on the symposium "On the Current State of Research in the Area of

Psychoactive Substances." In: C. Rätsch (Ed.) *The Gateway to Inner Space: A Festschrift in Honor of Albert Hofmann*. Bridport, England: Prism Press.

Meyer, P. 1992. Apparent communication with discarnate entities induced by dimethyltryptamine (DMT). *Jahrbuch für Ethnomedizin und Bewußtseinsforschung* 1: 149–174. Reprint, 1994. In: T. Lyttle (Ed.) *Psychedelics*. New York: Barricade Books.

Monardes, N. 1990. *Herbolaria de Indias*. México City: Redacta. Original 1569; English translation 1574 (reprint 1925). *Joyfull Newes Out of the Newe Founde Worlde*. London: Constable & Co.; New York: A.A. Knopf.

Moore, M. 1989. *Medicinal Plants of the Desert and Canyon West*. Santa Fe: Museum of New México Press.

Naranjo, C. 1967. Psychotropic properties of the harmala alkaloids. In: D.H. Efron; B. Holmstedt & N.S. Kline (Eds.) *Ethnopharmacologic Search for Psychoactive Drugs*. Washington, D.C: U.S. GPO.

Novaes da Mota, C. 1987. *As Jurema Told Us: Kariri-Shoko and Shoko Mode of Utilization of Medicinal Plants in the Context of Modern Northeastern Brazil*. Thesis, Austin: University of Texas. *Dissertation Abstracts* 48 (5): 1244-A.

Oga, S.; de Freitas, P.C.D.; Gomes da Silva, A.C. & Hanada, S. 1984. Pharmacological trials of crude extract of *Passiflora alata*. *Planta Medica* 50: 303–06.

Ott, J. 1997. *Pharmacophilia or The Natural Paradises*. Kennewick: Natural Products Co.

Ott, J. 1996. Pharmahuasca: On phenethylamines and potentiation. *MAPS Bulletin* VI (3): 32–35.

Ott J. 1995a. Ayahuasca e analoghi dell'ayahuasca: Enteogeni universali per il nuovo millennio. *Altrove* 2: 14–23. (Also in English, 1995. *Jahrbuch für Ethnomedizin und Bewußtseinsforschung* 3: 285–293.)

Ott, J. 1995b. Ethnopharmacognosy and human pharmacology of *Salvia divinorum* and salvinorin A. *Curare: Zeitschrift für Ethnomedizin* 18 (1): 103–29.

Ott, J. 1995c. Ayahuasca—Ethnobotany, phytochemistry and human pharmacology. *Integration: Zeitschrift für Geistbewegende Pflanzen und Kultur* 5: 72–98.

Ott, J. 1995d. *The Age of Entheogens & The Angels' Dictionary*. Kennewick: Natural Products Co.

Ott, J. 1994. *Ayahuasca Analogues: Pangæan Entheogens*. Kennewick: Natural Products Co. (German translation, 1995. *Ayahuasca Analoge: Pangæische Entheogene*. Löhrbach, Germany: MedienXperimente.)

Ott, J. 1996 [1993]. *Pharmacotheon: Entheogenic Drugs, Their Plant Sources and History*. Revised edition. Kennewick: Natural Products Co. (Castillian translation, 1996. *Pharmacotheon: Drogas Enteógenas, sus Fuentes Vegetales y su Historia*. Barcelona: Los Libros de la Liebre de Marzo.)

Pachter, I.J.; Zacharias, D.E. & Ribeiro, O. 1959. Indole alkaloids of *Acer saccharinum* (the silver maple), *Dictyoloma incanescens*, *Piptadenia colubrina*, and *Mimosa hostilis*. *Journal of Organic Chemistry* 24: 1285–87.

Poisson, J. 1965. Note sur le "Natem", boisson toxique péruvienne et ses alcaloïdes. *Annales Pharmaceutiques Françaises* 23 (4): 241–44.

Resnick, O.; Krus, D.M. & Raskin, M. 1964. LSD-25 action in normal subjects treated with a monoamine-oxidase inhibitor. *Life Sciences* 3 (11): 1207–14.

Rivier, L. & Lindgren, J.-E. 1972. "Ayahuasca," the South American hallucinogenic drink: An ethnobotanical and chemical investigation. *Economic Botany* 26 (1): 101–29.

Sai-Halász, A. 1963. The effect of MAO inhibition on the experimental psychosis induced by dimethyltryptamine. *Psychopharmacologia* 4 (6): 385–88.

Sai-Halász, A. 1962. The effect of antiserotonin on the experimental psychosis induced by dimethyltryptamine. *Experientia* 18 (3): 137–38.

Sai-Halász, A.; Brunecker, G. & Szára, S. 1958. Dimethyltryptamin: Ein neues Psychoticum. *Psychiatria et Neurologia* 135: 285–301.

Schultes, R.E. & Hofmann, A. 1980. *The Botany and Chemistry of Hallucinogens*. Second edition, revised. Springfield: C.C. Thomas.

Shamma, A. al- & Abdul-Ghany, A.-M. 1977. A comparative study of the alkaloidal contents of *Peganum harmala* L. *Bulletin of the Biology Research Center, Baghdad* 8: 10–16.

Shulgin, A.T. 1993. Personal communications, Madrid, Spain and Maui, HI.

Shulgin, A.T. 1983. Cited in: P.A.G.M. de Smet. A multidisciplinary overview of intoxicating enema rituals in the western hemisphere. *Journal of Ethnopharmacology* 9 (2,3): 129–66.

Shulgin, A.T. 1976. Profiles of psychedelic drugs. 1. DMT. *Journal of Psychedelic Drugs* 8 (2): 167–68.

Shulgin, A.T. 1970. Chemistry and structure-activity relationships of the psychotomimetics. In: D.H. Efron (Ed.) *Psychotomimetic Drugs*. New York: Raven Press.

Shulgin, A.T. & Shulgin, A. 1997. *TIHKAL: The Continuation*. Berkeley: Transform Press.

Shulgin, A.T. & Shulgin, A. 1991. *PIHKAL: A Chemical Love Story*. Berkeley: Transform Press.

Siebert, D.J. 1994. *Salvia divinorum* and salvinorin A: New pharmacologic findings. *Journal of Ethnopharmacology* 43 (1): 53–56.

Smith, T.A. 1977. Tryptamine and related compounds in plants. *Phytochemistry* 16:171–75.

Speroni, E. & Minghetti, A. 1988. Neuropharmacological activity of extracts from *Passiflora incarnata*. *Planta Medica* 54:488–91.

Strassman, R.J. & Qualls, C.R. 1994. Dose-response study of N,N-dimethyltryptamine in humans I. Neuroendocrine, autonomic, and cardiovascular effects. *Archives of General Psychiatry* 51:85–97.

Strassman, R.J.; Qualls, C.R.; Uhlenhuth, E.H. & Kellner, R. 1994. Dose-response study of N,N-dimethyltryptamine in humans II. Subjective effects and preliminary results of a new rating scale. *Archives of General Psychiatry* 51:98–108.

Szára, S.I. 1957. The comparison of the psychotic effect of tryptamine derivatives with the effects of mescaline and LSD-25 in self-experiments. In: S. Garattini & V. Ghetti (Eds.) *Psychotropic Drugs*. Amsterdam: Elsevier.

Turner, W.J. & Merlis, S. 1959. Effect of some indolealkylamines on man. *Archives of Neurology and Psychiatry* 81:121–29.